PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

Dr. Daniel C. JAVITT

Appln. No.: 09/320,446

Confirmation No.: 4739 Group Art Unit: 1627

Filed: May 27, 1999 Examiner: Ponnaluri

For: GLYCINE SITE FULL AGONIST FOR TREATING A PSYCHOSIS

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to examination, please amend the above-identified application as follows:

IN THE TITLE:

The title is changed as follows:

GLYCINE SUBSTITUTES AND PRECURSORS FOR TREATING A PSYCHOSIS

IN THE SPECIFICATION:

Amend the specification by inserting before the first line the sentence:

This is application is a continuation application of prior continuation-in-part application 09/320,446 filed May 27, 1999, which is a continuation -in-part application of 09/212,273 filed December 16, 1998 (now U.S. patent 6,162,827) in turn a divisional application of 08/759,714

filed December 6, 1996 (now U.S. patent 5,854,286). Priority is claimed from Provisional application 60/008361 filed December 7, 1995. The subject matters of the prior applications are incorporated in their entirety herein by reference thereto.

Page 3, between lines 18 and 19 insert the following:

--**BRIEF DESCRIPTION OF THE DRAWING**

Figure 1 plots negative symptom levels derived from the Positive and Negative Syndrome Scale (PANSS) for subjects during treatment with glycine and D-cycloserine. Circles represent individuals treated with conventional antipsychotics (open circles) or clozapine (closed circles). Bars represent group means.

Figure 2 depicts effects of glycyldodecylamide (GDA) on locomotor hyperactivity induced by phencyclidine (PCP) or amphetamine. Bars are mean $\pm$ s.e.m. ***$p<.001$ vs. ctl

Figure 3 depicts effect of a series of glycineamide derivatives on locomotor hyperactivity induced by PCP. All agents were given at a does of 100 mg/kg. Bars are mean $\pm$ s.e.m. *$p<.05$ vs. ctl. **$p<.01$ vs. ctl

Figure 4 depicts inhibition of [^{3}H]glycine transport (glycine uptake) in P2 synaptosomal fractions by indicated concentrations of glycineamide derivatives.

Figure 5 is a scatter plot showing the relationship between potency in reducing PCP-induced hyperactivity in vivo and potency in inhibiting synaptosomal glycine uptake in vitro. For in vivo experiments, agents were tested at a dose of 100 mg/kg. For uptake experiments, agents were tested at a dose of 100 µg/ml.--

Page 14, lines 15-16, delete and insert the following:

Leiderman E, Zylberman I, Javitt DC, Zukin SR, Cooper TB. Effect of high-dose oral glycine on serum levels and negative symptoms in schizophrenia. Biol. Psychiatry,1996; 39:213-215.

IN THE CLAIMS:

Please cancel claims 1-8 without prejudice or disclaimer.

Please add the following new claim:

9. (New) A process for providing glycine for delivery to the central nervous system of a human patient which comprises microencapsulating the glycine in liposomes and administering the liposomes to the patient.

IN THE ABSTRACT:

On page 19, delete the abstract and insert the following new abstract:

Process for treating psychosis such as schizophrenia using a glycine substitute or a precursor thereof to potentiate NMDA receptor-mediated neurotransmission

REMARKS

Entry and consideration of this Amendment is respectfully requested.

Respectfully submitted,

Louis Gubinsky
Registration No. 24,835

SUGHRUE MION, PLLC
2100 Pennsylvania Avenue, N.W.
Washington, D.C. 20037-3213
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

Date: January 31, 2002

APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE TITLE:

The title is changed as follows:

~~GLYCINE SITE FULL AGONIST FOR TREATING A PSYCHOSIS~~GLYCINE SUBSTITUTES AND PRECURSORS FOR TREATING A PSYCHOSIS

IN THE SPECIFICATION:

The specification is changed as follows:

Amend the specification by inserting before the first line the sentence:

This is application is a continuation application of prior continuation-in-part application 09/320,446 filed May 27, 1999, which is a continuation of 09/212,273 filed December 16, 1998 (now U.S. patent 6,162,827) in turn a divisional application of 08/759,714 filed December 6, 1996 (now U.S. patent 5,854,286). Priority is claimed from Provisional application 60/008361 filed December 7, 1995. The subject matters of the prior applications are incorporated in their entirety herein by reference thereto.

Page 3, between lines 18 and 19 insert the following:

--**BRIEF DESCRIPTION OF THE DRAWING**

Figure 1 plots negative symptom levels derived from the Positive and Negative Syndrome Scale (PANSS) for subjects during treatment with glycine and D-cycloserine. Circles

represent individuals treated with conventional antipsychotics (open circles) or clozapine (closed circles). Bars represent group means.

Figure 2 depicts effects of glycyldodecylamide (GDA) on locomotor hyperactivity induced by phencyclidine (PCP) or amphetamine. Bars are mean + s.e.m. ***p<.001 vs. ctl

Figure 3 depicts effect of a series of glycineamide derivatives on locomotor hyperactivity induced by PCP. All agents were given at a does of 100 mg/kg. Bars are mean + s.e.m. *p<.05 vs. ctl. **p<.01 vs. ctl

Figure 4 depicts inhibition of [^{3}H]glycine transport (glycine uptake) in P2 synaptosomal fractions by indicated concentrations of glycineamide derivatives.

Figure 5 is a scatter plot showing the relationship between potency in reducing PCP-induced hyperactivity in vivo and potency in inhibiting synaptosomal glycine uptake in vitro. For in vivo experiments, agents were tested at a dose of 100 mg/kg. For uptake experiments, agents were tested at a dose of 100 µg/ml.--

Page 14, lines 15-16, delete and insert the following:

Leiderman E, Zylberman I, Javitt DC, Zukin SR, Cooper TB. Effect of high-dose oral glycine on serum levels and negative symptoms in schizophrenia. Biol. Psychiatry, ~~in press~~1996; 39:213-215.

IN THE CLAIMS:

Claims 1-8 are canceled.

Claim 9 is added as new claim.

9. (New) A process for providing glycine for delivering to the control nervous system of a human patient which comprises microencapsulating the glycine in liposomes and administering the liposomes to the patient.

IN THE ABSTRACT:

On page 19, delete the abstract and insert the following new abstract:

Process for treating psychosis such as schizophrenia using ~~glycine site full agonist~~ a glycine substitute or a precursor thereof to potentiate NMDA receptor-mediated neurotransmission.